

In response to Reviewer 1

Comments to the authors: I think the draft is a little unreadable, including many syntaxes and word uncommon uses.

Response: We appreciate the complimentary comments from the reviewer. Thank you for spending your valuable time reviewing the manuscript. The paper has been carefully revised, and the language was polished.

Comments to the authors: I think authors should address the puzzles of organ transplantation, for example, IRI, donor age, DCD, fatty liver, etc, and how does machine perfusion improve them.

Response: We appreciated the suggestion from the reviewer. We believe that the manuscript covered all the mentioned topics within the methodological limitations of the article type as provided by the journal (a Frontier article). Detailed and profound discussion of each topic is beyond the scope of the manuscript and would require a comprehensive review.

Reviewer 2

Comments to the authors: I suggest expanding this section since it represents a critical point with regard to dynamic preservation and/or regeneration. In fact, bile duct cells seem more resistant to hypoxia in comparison with hepatocytes (at list when they are prepared for cell cultures) on the other hand several data underscore that a valid preservation of peri-biliary plexus and glands is likely the most important factor for the biliary tract injury repair, after ischemia (PMID: 30506902). In this perspective future studies on machine perfusion should have, among other targets, the aim to maintain a healthy peri-biliary environment rather than focusing on biliary cells viability, in order to favour graft recovery after transplant. Please include these points in the manuscript.

Response: We thank the reviewer for the thoughtful analysis of the work. In accordance, the importance of maintaining a healthy microenvironment for peribiliary glands during machine perfusion and its implications were discussed in the manuscript. Please see page 08 of the revised manuscript.

Comments to the authors: I suggest to include a table (with references) summarizing the suggested parameters to dynamically assess organ viability during different perfusion techniques.

Response: We highly appreciate the reviewer's comment. In accordance, a table summarising parameters used in clinical studies to assess organ viability during machine perfusion of the liver was included.

Comments to the authors: Figure 1: I would suggest to remove the arrows from x and y axis. I would suggest also the following changes: title "organ preservation" instead of "dynamic organ preservation"; box titles: "adverse environment" change with "Past"; "favourable environment" change with "Present".

Response: We thank the reviewer for the recommendation. All the suggested changes in Figure 1 were accepted and adopted by the authors.